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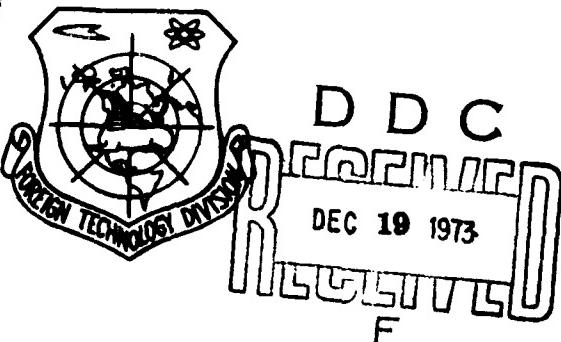
## FOREIGN TECHNOLOGY DIVISION



ANAPHYLACTOGENIC AND IMMUNOGENIC  
PROPERTIES OF LOWER FUNGI

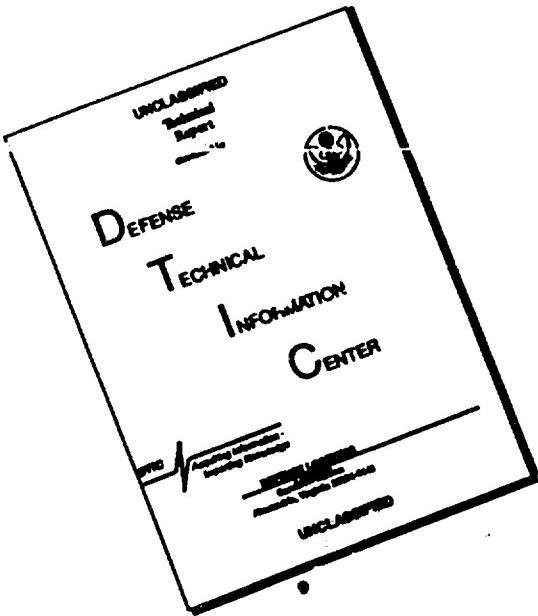
BY

N. I. Pasternak, V. G. Brysin



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By: N. I. Pasternak, V. G. Brysin

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## ANAPHYLACTOGENIC AND IMMUNOGENIC PROPERTIES OF LOWER FUNGI

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imeni M. I. Kalinin

Sensitization by fungi spores at the present time is considered as an important and most frequent factor in the development of allergic processes [5-8]. It is considered that sensitization by fungus air-dust flora which is to blame for wide allergizing of the population [4] should not be identified with fungus infection nor with allergies with fungus illnesses. Spores of fungi, as dusts of plants which have penetrated the nasal tract in an organism, without subsequent growth and reproduction in tissues serve to develop allergic alteration [1]. There is evidence of significant distribution of sensitization to fungus flora and its participation in the onset of bronchial asthma, rhinitis, and conjunctivitis [2]. Allergy to the lower fungi is the least studied type of allergic pathology. Single papers [2, 6] have been devoted to the study of the anaphylactic properties of mould fungi [3] as well as to discovering circulating antibodies against fungus antigens in the blood of patients.

Procedure. We made a study of the anaphylactic and immunogenic properties of fungi *Candida trop.*, *Alternaria* sp., *Aspergillus* fl., and *Cladosporium* sp. For the tests use was made of anaphylactic shock, anaphylactic contracture of a section of intestine according to Schultz-Dale, and also fixation reactions of a complement (to cold), reactions of passive hem-agglutination according to Boyden, and reactions of precipitation in gel according to Ochterlony.

Cultures of fungi were cultivated in Chayka's agar with cellophane. Extracts of fungi were prepared in an Evans-Koch<sup>1</sup> alcoholic liquid. In the prepared extracts we determined the content of albumin nitrogen (according to Lowry), total and albumin nitrogen (according to micro-Kjeldal). On 12 guinea pigs and 20 mice possible secondary effect and toxicity of the extracts were excluded.

In order to study the possibility of reproduction of anaphylactic shock, 60 pigs were sensitized twofold with a two-day interval with fungus extract with full Freund adjuvant (0.2 ml each). In 21 days, to the pigs a resolving dose (1.0 ml) of the extract of the corresponding fungus was administered. Anaphylactic shock was estimated according to the degree of severity with computation of the anaphylactic index (AI) according to Begly.

The pigs (20) used for the study of anaphylactic contracture of a section of intestine were sensitized by 1 and 3 subcutaneous injections of fungus extract with full adjuvant (0.2 ml) and with intraperitoneal administration (2nd injection) of fungus

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<sup>1</sup>Presented at the All-Union conference on preparation, approbation, and control of allergens (Moscow, 1969).

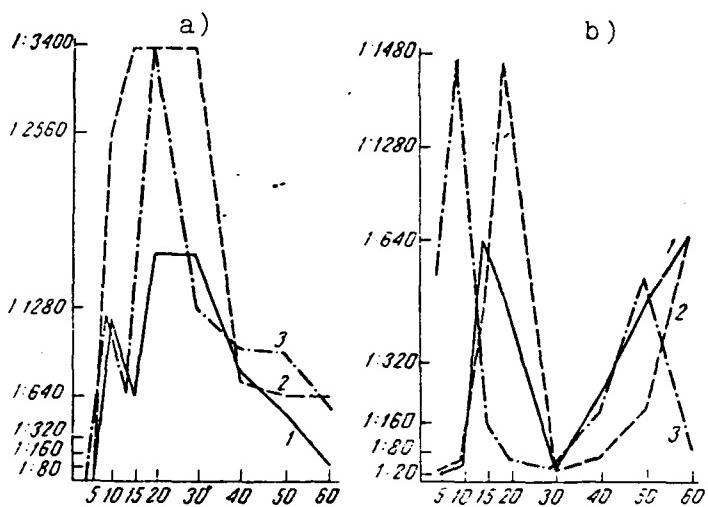
extract (0.2 ml). The pigs were killed by bleeding on the 25th-30th day after the conclusion of sensitization. Carefully, the jejunal and iliac intestines were separated and cut into sections 1.5-2 cm in length, and after 25-30 minutes of adaptation in an oxygenated Tyrode solution (37°) were used in the experiment. The viability of a section of intestine was determined according to sensitivity to histamine ( $10^{-9}$ ). On a section of intestine of intact pigs the possible non-specific action of the fungus extracts used was excluded.

The dynamics of the titre of antibodies circulating in the blood was studied on 27 rabbits which were sensitized subcutaneously with 5% suspension of spores of the corresponding fungus with full adjuvant. After completion of sensitization, on the 5, 10, 15, 20, 30, 40, 50, and 60th day, blood was taken from the peripheral vein of the ear for serological studies. As an antigen in the serological reactions, a 5% extract of the corresponding fungus was used - undiluted and in dilutions.

Results. Intravenous resolving administration to sensitized pigs of an extract of fungus Candida (1), Aspergillus (2), Alternaria (3), and Cladosporium (4) caused the development of anaphylactic shock of various degree of severity. Some of the pigs died of shock. According to the severity of the induced shock, the fungus extracts used were distributed:  $AI_1 = 3.0$ ;  $AI_2 = 2.5$ ;  $AI_3 = 2.3$ ;  $AI_4 = 2.6$ . The most pronounced anaphylactic properties were possessed by the extract of fungus Candida, the least pronounced - by Alternaria. Perfusion of a specific fungus extract through the working beaker of a Schultz-Dale apparatus containing a smooth muscle preparation of a sensitized pig caused the development of anaphylactic contracture of the section of isolated intestine.

The precipitation reaction in gel to the studied types of fungi precipitating antibodies was not observed. However,

hemagglutinating (see Fig. a) and complement-fixating (Fig. b) antibodies were observed.



Dynamics of titre of hemagglutinating (a) and complement-fixating (b) antibodies in fungus sensitization. 1 - *Alternaria* sp.; 2 - *Candida* tr.; 3 - *Aspergillus* fl.  
On axis of abscissa - days of study; on axis of ordinates - titre of antibodies.

In the dynamics of titre of hemagglutinating antibodies against the fungi Aspergillus, Alternaria, a definite generality was observed. Antibodies against these fungi were revealed in low titre (1:20) by the 5th day, which increased (1:1280) by the 10th, and reduced (to 1:640) by the 15th day. By the 20th day the titre of hemagglutins again rose. Against the fungus Alternaria the maximum titre comprised 1:1600, against the fungus Aspergillus - 1:3400. Then the titre of antibodies gradually, up to the 60th day, was reduced: against the fungus Alternaria to 1:160; against the fungus Aspergillus to 1:640, i.e., it remained high. The dynamics of titre of antibodies against the fungus Candida had a somewhat different character. On the 5th day they were observed at low titre (1:20); on the 10th day the titre rose to 1:2560. For hemagglutins against the fungus Candida characteristic was the prolonged presence in the blood at high titre (1:3400), a gradual

lowering by the 60th day to 1:640. Hemagglutins against all forms of the studied fungi reached highest titre by the 15-20th day, gradually lowering to the 60th.

Complement-fixating antibodies against the fungus Alternaria on the 5th day were revealed at low titre (1:20), increased insignificantly (to 1:40) by the 10th day, reaching a maximum (1:640) by the 15th day. By the 30th day, the titre of these antibodies against the fungus Alternaria dropped to 1:40, rose again (to 1:640) by the 60th day. Against the fungus Candida on the first days antibodies were revealed at low dilutions, gradually reaching high titre (1:1480) by the 20th day, by the 30th their titres were sharply reduced, and by the 60th day again rose, being however, lower than on the 20th day. Antibodies against the fungus Aspergillus even on the 5th day were determined at high titre (1:560), reaching a maximum (1:1480) by the 10th day. By the 30th day, titre of antibodies against the fungus Aspergillus gradually lowered, reaching 1:40, and again rose (to 1:560) by the 50th day, again lowering (1:80) on the 60th day. In this way, for complement-fixating antibodies characteristic is a wave-like character of their being in the blood. For these antibodies against fungi Candida and Alternaria in the course of 60 days, 2 periods of increased titre were observed. Against the fungus Alternaria, the titre of antibodies by the 60th day reached that same level as in the first period of its rise (on the 15th day). The titre of antibodies against the fungus Candida rose significantly by the 60th day without reaching the level observed in the first period of rise. Against the fungus Aspergillus, 2 periods of rise and reduction of titre of antibodies were noted.

For hemagglutins against antigens of the fungi Alternaria and Candida also a wave-like increase of titre is characteristic (see figure). The dynamics of hemagglutinating and complement-fixating of antibodies are of the same type, although against

the fungus Alternaria the titre of antibodies was significantly lower.

And thus, extracts of fungi Candida trop., Alternaria sp., Aspergillus fl., Cladosporium sp., posses anaphylactic properties. Sensitization of rabbits by the lower fungi causes the production of hemagglutinating and complement-fixating antibodies, the dynamics of the titre of which has a wave-like character.

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